```
=> fil reg; d stat que l27; fil capl; d que nos l28
FILE 'REGISTRY' ENTERED AT 12:12:40 ON 18 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   16 MAR 2002  HIGHEST RN 401560-75-6
DICTIONARY FILE UPDATES:  16 MAR 2002  HIGHEST RN 401560-75-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02.  Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved.  Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies.  Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.
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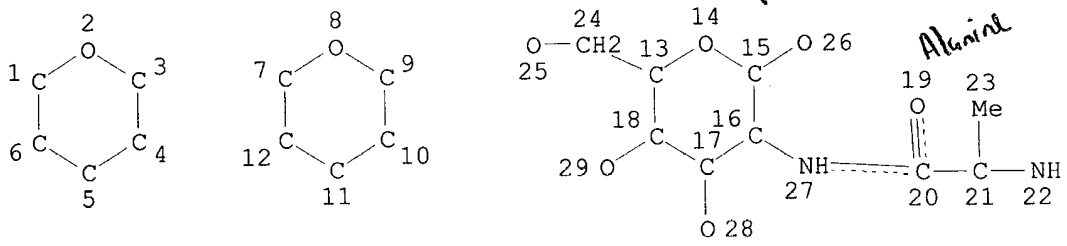
L24 STR

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  29

STEREO ATTRIBUTES: NONE
L27          11 SEA FILE=REGISTRY SSS FUL L24

100.0% PROCESSED   2083 ITERATIONS                    11 ANSWERS
SEARCH TIME: 00.00.01
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FILE 'CAPLUS' ENTERED AT 12:12:40 ON 18 MAR 2002

FILE COVERS 1907 - 18 Mar 2002 VOL 136 ISS 12
FILE LAST UPDATED: 15 Mar 2002 (20020315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

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L24             STR
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L28           6 SEA FILE=CAPLUS ABB=ON  L27
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crossover of Registry answer set into CAPLUS to get citations

=> d ibib abs hitstr l28 1-6; fil uspatf; d que nos l29; fil caold; d que nos l30

L28 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:222817 CAPLUS
DOCUMENT NUMBER: 133:2301
TITLE: Structural characterization of the outer core and the O-chain linkage region of lipopolysaccharide from Pseudomonas aeruginosa serotype O5
AUTHOR(S): Sadovskaya, Irina; Brisson, Jean-Robert; Thibault, Pierre; Richards, James C.; Lam, Joseph S.; Altman, Eleonora
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, K1A 0R6, Can.
SOURCE: Eur. J. Biochem. (2000), 267(6), 1640-1650
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The point of attachment of the O-chain in the outer core region of Pseudomonas aeruginosa serotype O5 lipopolysaccharide (LPS) was detd.

following a detailed anal. of the extended core oligosaccharide, contg. one trisaccharide O-chain repeating unit, present in both the wild-type strain PAO1 and O-chain deficient mutant strains AK1401 and PAO-rfc. The structure of the extended core oligosaccharide was detd. by various mass spectrometric methods as well as one-dimensional and two-dimensional NMR spectroscopy. Furthermore, the one-dimensional analogs of NOESY and TOCSY expts. were applied to confirm the structure of the outer core region in the O-chain polysaccharide. In both the extended core oligosaccharide and the core of the smooth LPS, a loss of one of the .beta.-glucosyl residues and the translocation of the .alpha.-rhamnosyl residue, followed by the attachment of the first O-chain repeating unit was obsd. This process is complicated and could involve two distinct rhamnosyltransferases, one with .alpha.-1,6-linkage specificity and another with .alpha.-1,3-linkage specificity. It is also plausible that an .alpha.-1,3 rhamnosyltransferase facilitates the addn. of the new .alpha.-rhamnosyl residue that will act as a receptor for the attachment of the single O-antigen repeating unit in the LPS of the semi-rough mutant. The 2-amino-2-deoxy-fucosyl residue of the first O-chain repeating unit directly attached to the core was found to have a .beta.-anomeric configuration instead of an .alpha. configuration, characteristic for this residue as a component of the O-chain polysaccharide. The results of this study provide the first example of the mechanistic implications of the structure of the outer core region in a fully assembled O-chain-contg. LPS, differing from the O-chain deficient rough LPS.

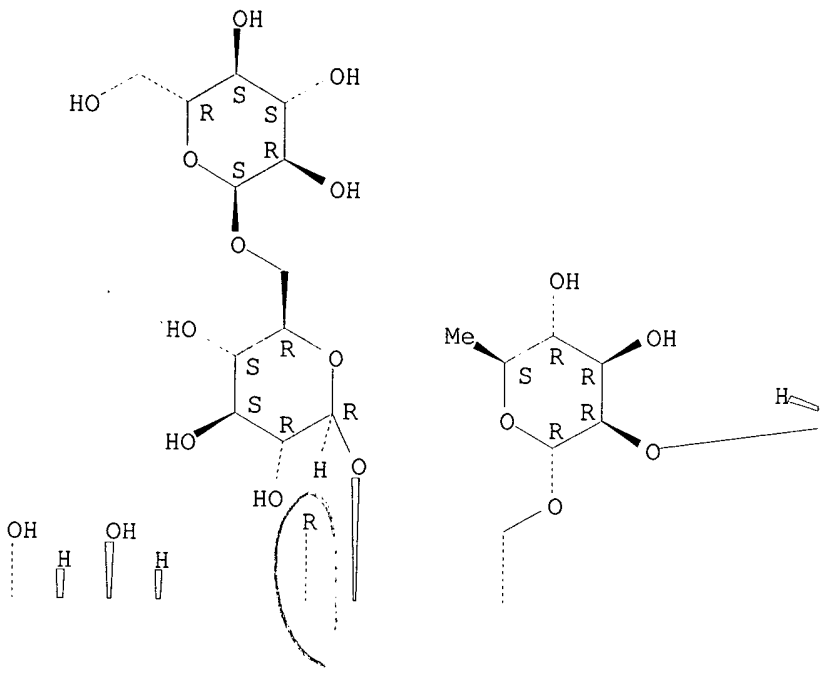
IT **271261-32-6**
RL: PRP (Properties)
(structure of the core oligosaccharide of lipopolysaccharide from Pseudomonas aeruginosa serotype O5)

RN 271261-32-6 CAPLUS

CN D-manno-2-Octulosonic acid, O-.beta.-D-glucopyranosyl-(1.fwdarw.2)-O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.6)-O-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-[O-.alpha.-D-glucopyranosyl-(1.fwdarw.6)-.beta.-D-glucopyranosyl-(1.fwdarw.3)]-O-2-[[(2S)-2-amino-1-oxopropyl]amino]-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.3)-O-7-O-(aminocarbonyl)-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.3)-O-2,4,6-tri-O-phosphono-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.5)-3-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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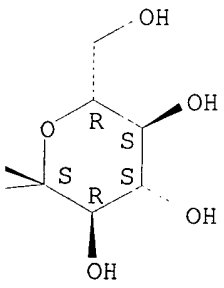

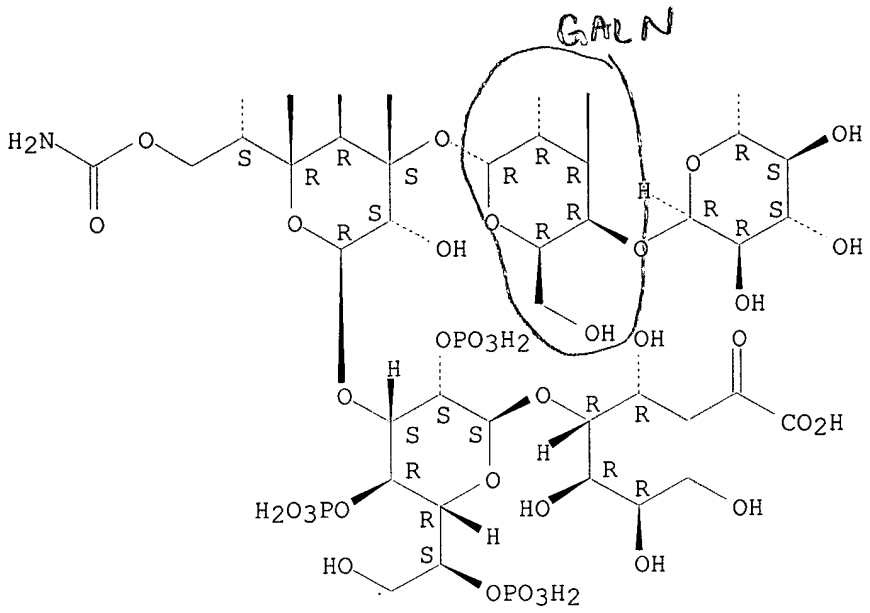

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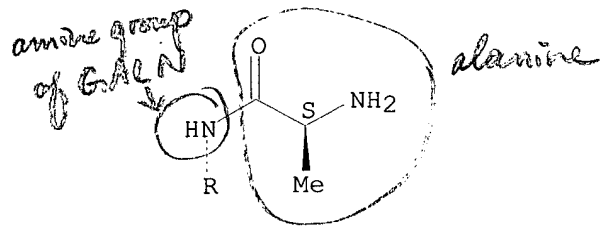


PAGE 3-A

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:791476 CAPLUS
DOCUMENT NUMBER: 130:92442
TITLE: Enhancement of sample loadings for the analysis of oligosaccharides isolated from Pseudomonas aeruginosa using transient isotachophoresis and capillary zone electrophoresis-electrospray-mass spectrometry
AUTHOR(S): Auriola, Seppo; Thibault, Pierre; Sadovskaya, Irina; Altmann, Eleonora
CORPORATE SOURCE: Faculty Pharmacy, University Kuopio, Kuopio, Finland
SOURCE: Electrophoresis (1998), 19(15), 2665-2676
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anal. of underivatized core oligosaccharides arising from mild acid hydrolysis of lipopolysaccharides from Pseudomonas aeruginosa serotype 05 was achieved using a transient isotachophoretic preconcn. method coupled to capillary zone electrophoresis-electrospray-mass spectrometry (tCITP-CZE-ES-MS). The combination of a tCITP preconcn. step provided a 10- to 50-fold enhancement of sample loading and a corresponding improvement in sensitivity compared to the conventional zone electrophoresis format. Electrophoretic conditions, enabling the sepn. of these anionic analytes, were developed to det. possible sites of heterogeneity on either the core or the O-chain structures. The tCITP-CZE-ES-MS technique provided unparalleled resoln. of the different

core glycoforms and oligosaccharides obtained from the acid cleavage of the native endotoxins whether isolated following conventional gel permeation chromatog. or obtained from direct hydrolysis of the bacterial isolates. These investigations also highlighted the highly phosphorylated nature of these complex cell membrane components, where the heptose residues of the core oligosaccharide can bear up to 6 phosphate groups.

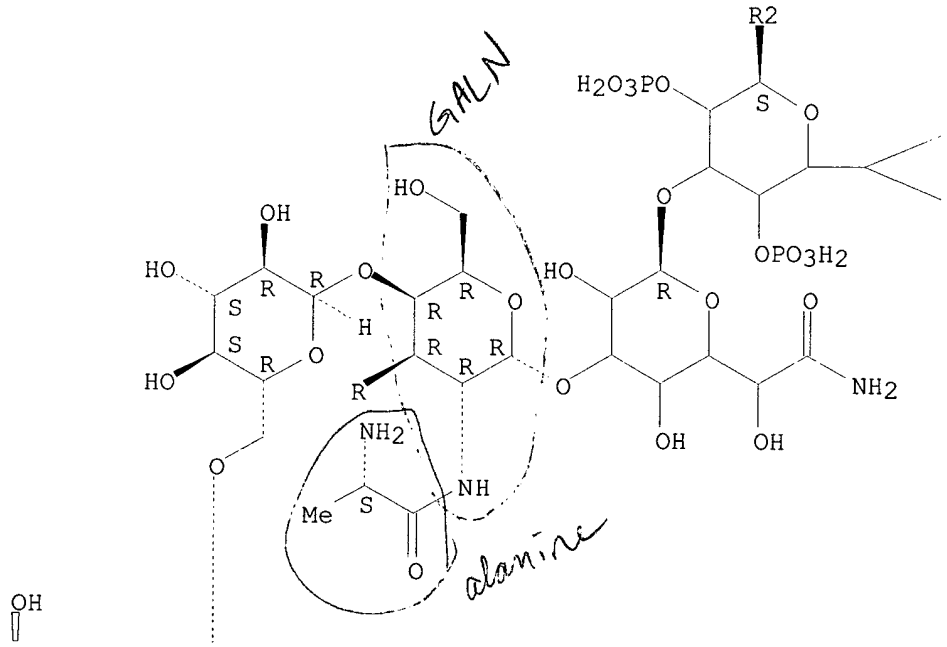
IT **219138-40-6D**, lipid-A contg.
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(enhancement of sample loadings for the anal. of oligosaccharides isolated from Pseudomonas aeruginosa using transient isotachophoresis and capillary zone electrophoresis-electrospray-mass spectrometry)

RN 219138-40-6 CAPLUS

CN .alpha.-D-manno-2-Octulopyranosonic acid, O-3-deoxy-.alpha.-D-manno-2-octulopyranosonosyl-(2.fwdarw.4)-O-[O-.beta.-D-glucopyranosyl-(1.fwdarw.2)-O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.6)-O-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-[O-.beta.-D-glucopyranosyl-(1.fwdarw.6)-.beta.-D-glucopyranosyl-(1.fwdarw.3)]-O-2-[[(2S)-2-amino-1-oxopropyl]amino]-2-deoxy-.alpha.-D-galactopyranosyl-O-(1.fwdarw.3)-O-heptopyranuronamidosyl-(1.fwdarw.3)-2,4,6-tri-O-phosphonoheptopyranosyl-(1.fwdarw.5)]-3-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Currently available stereo shown.

PAGE 1-A



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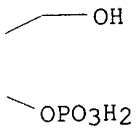

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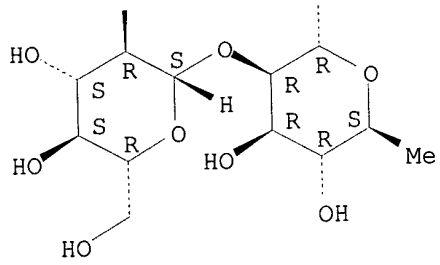

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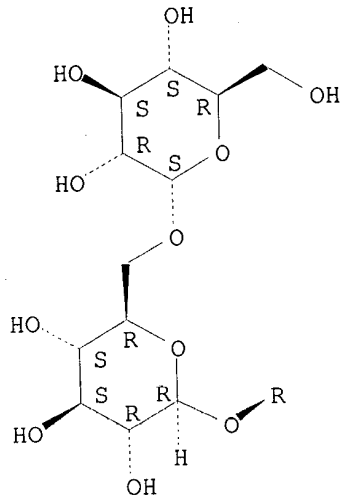

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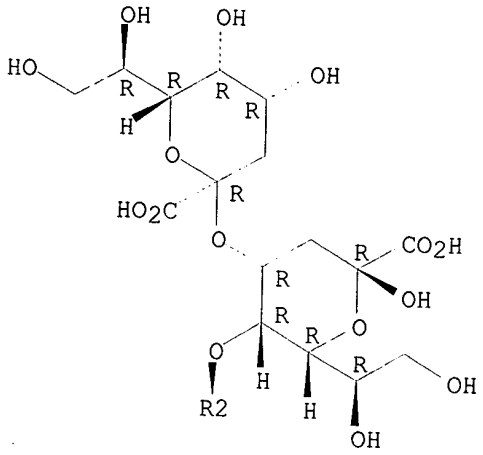


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:638884 CAPLUS
DOCUMENT NUMBER: 130:1530
TITLE: Structural elucidation of the lipopolysaccharide core regions of the wild-type strain PAO1 and O-chain-deficient mutant strains AK1401 and AK1012 from Pseudomonas aeruginosa serotype O5
AUTHOR(S): Sadovskaya, Irina; Brisson, Jean-Robert; Lam, Joseph S.; Richards, James C.; Altman, Eleonora
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, K1A OR6, Can.
SOURCE: Eur. J. Biochem. (1998), 255(3), 673-684
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

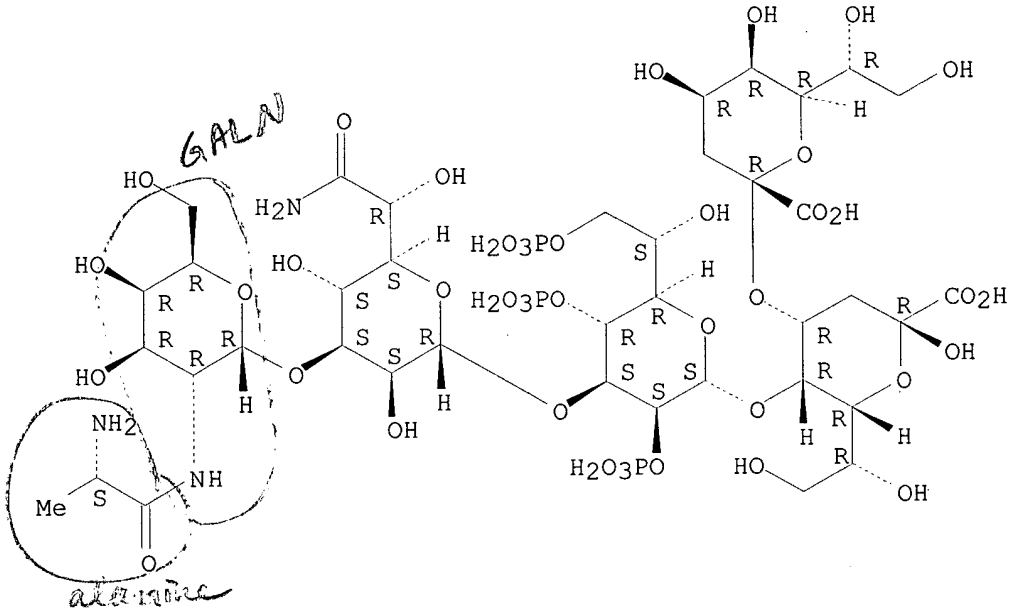
AB Lipopolysaccharide (LPS) of the Pseudomonas aeruginosa serotype O5 wild-type strain PAO1 and derived rough-type mutant strains AK1401 and AK1012 was isolated by a modified phenol/chloroform/petroleum-ether extn. method. Deoxycholate/PAGE of the LPS from the rough mutant AK1401 indicated two bands near the dye front with mobilities similar to those of the parent strain, indicating that both LPS contain a complete core and a species comprising a core and one repeating unit. Compn. anal. of the LPS from strains PAO1 and AK1401 indicated that the complete core oligosaccharide was composed of D-glucose (four units), L-rhamnose (one unit), 2-amino-2-deoxy-D-galactose (one unit), L-glycero-D-manno-heptose (Hep; two units), 3-deoxy-D-manno-octulosonic acid (Kdo; two units), L-alanine (one unit) and phosphate (three units). The glycan structure of the LPS was detd. by one-dimensional and two-dimensional (2D) NMR techniques in combination with MS-based methods on oligosaccharide samples obtained from the LPS by delipidation procedures. The locations of three phosphomonoester groups on the first heptose residue were established by a two-dimensional 31P (.omega.1)-half-filtered COSY expt. on the reduced core oligosaccharide sample of the LPS from the wild-type strain. The presence of a 7-O-carbamoyl substituent was obsd. on the second heptose. The structure of the core region of the O-chain-deficient LPS from P. aeruginosa serotype O5 is given. A structural model is presented that is also representative of that for P. aeruginosa serotype O6 LPS. A revised structure for the serotype O6 mutant strain A28 is presented.

IT **215672-18-7D**, reaction product with lipid A **215672-19-8D**

, reaction product with lipid A **215672-20-1D**, reaction product with lipid A **215672-21-2 215672-22-3**
RL: PRP (Properties)
(structural elucidation of the lipopolysaccharide core regions of the wild-type strain PAO1 and O-chain-deficient mutant strains AK1401 and AK1012 from Pseudomonas aeruginosa serotype O5)

RN 215672-18-7 CAPLUS
CN .alpha.-D-manno-2-Octulopyranosonic acid, O-2-[[(2S)-2-amino-1-oxopropyl]amino]-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.3)-O-L-glycero-.alpha.-D-manno-heptopyranuronamidosyl-(1.fwdarw.3)-O-2,4,7-tri-O-phosphono-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.5)-O-[3-deoxy-.alpha.-D-manno-2-octulopyranosonosyl-(2.fwdarw.4)]-3-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215672-19-8 CAPLUS
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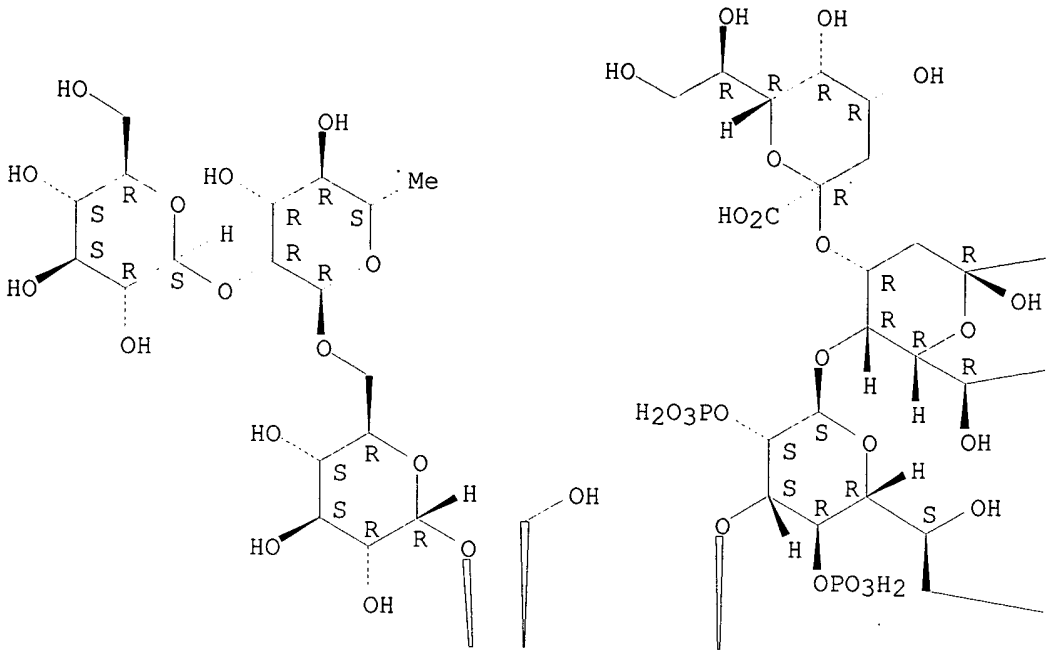
Absolute stereochemistry.

PAGE 1-A



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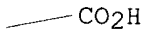

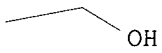

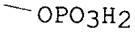

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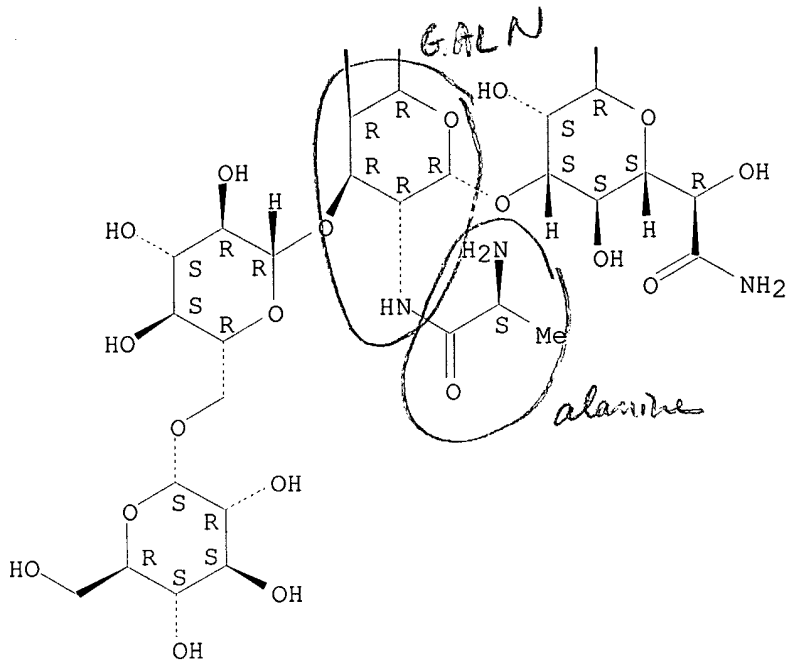

RN 215672-20-1 CAPLUS
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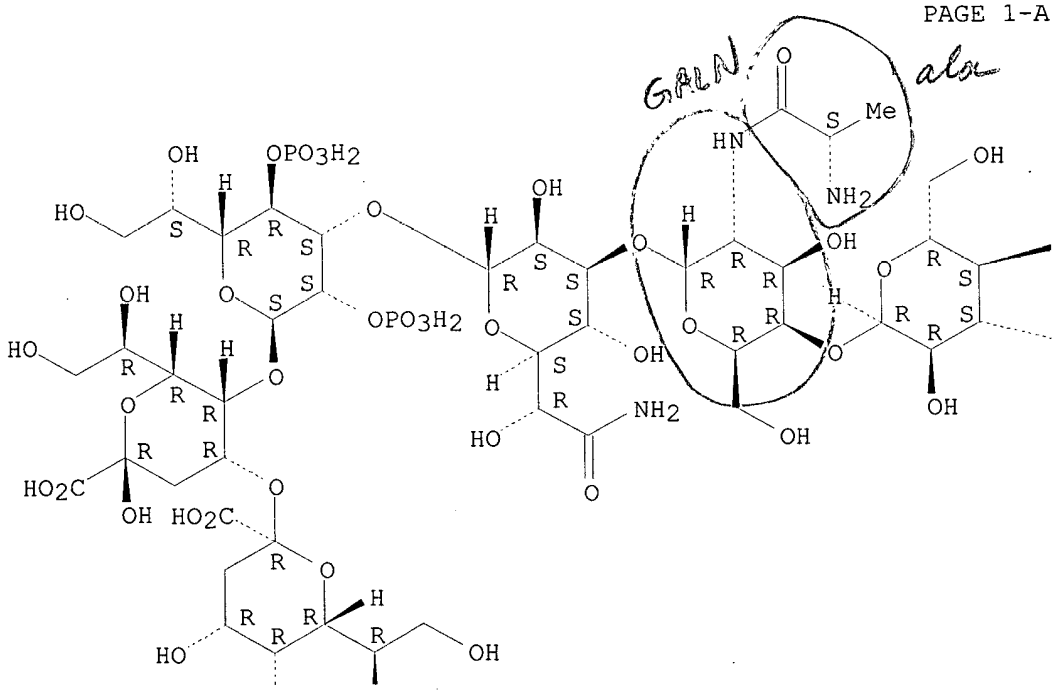
Absolute stereochemistry.

PAGE 1-A



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RN 215672-21-2 CAPLUS
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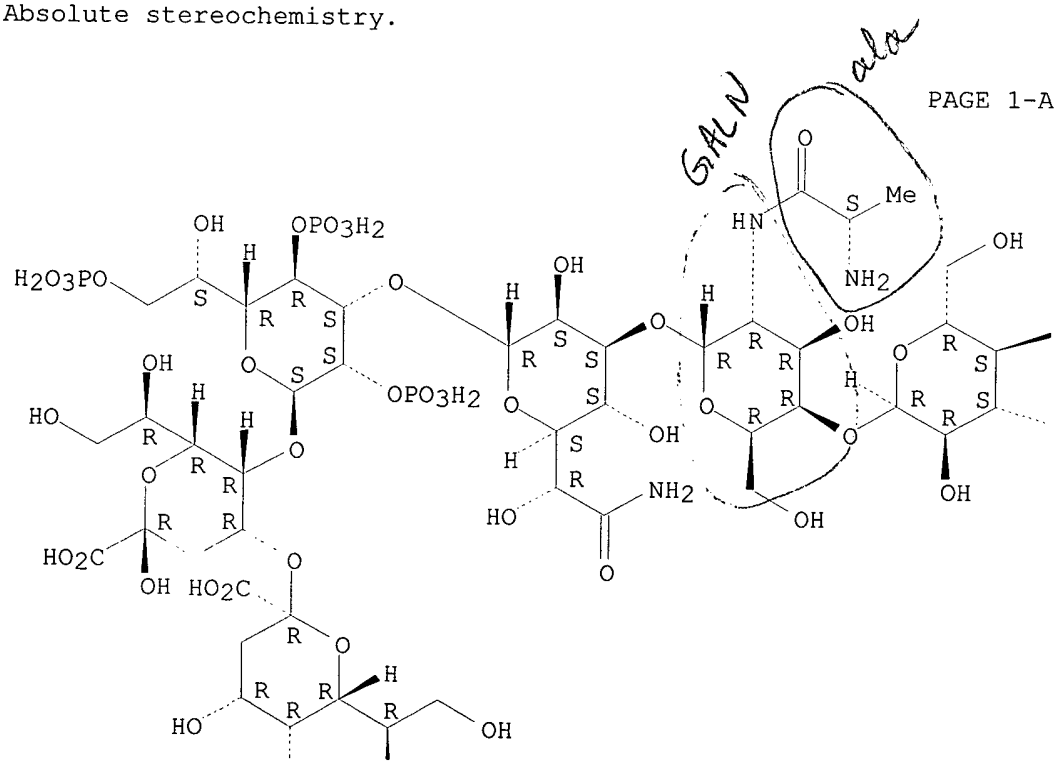
Absolute stereochemistry.

PAGE 1-A



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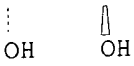
PAGE 2-A



RN 215672-22-3 CAPLUS
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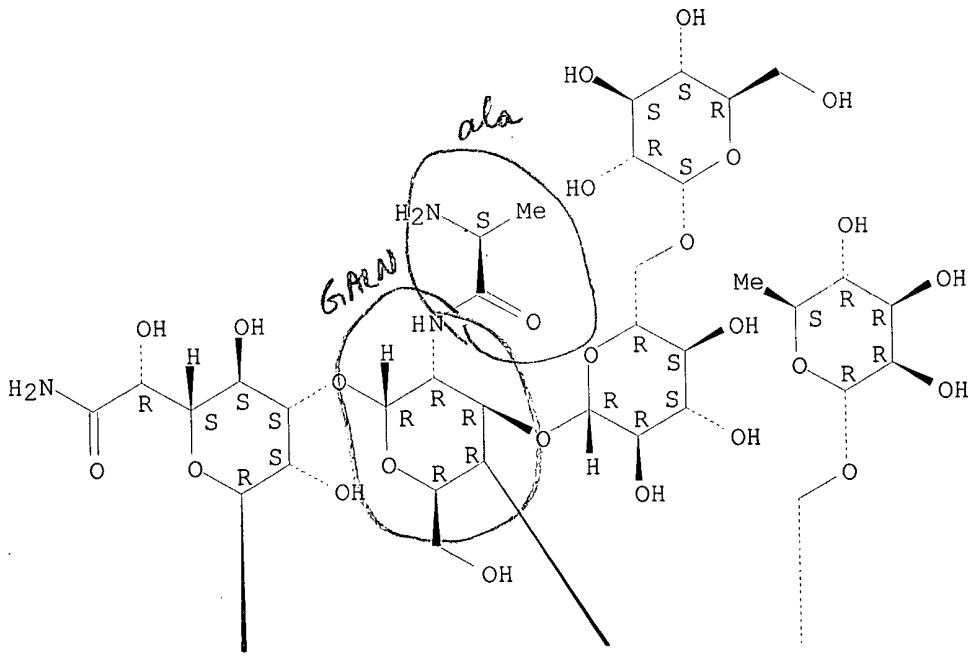
Absolute stereochemistry.

PAGE 1-A



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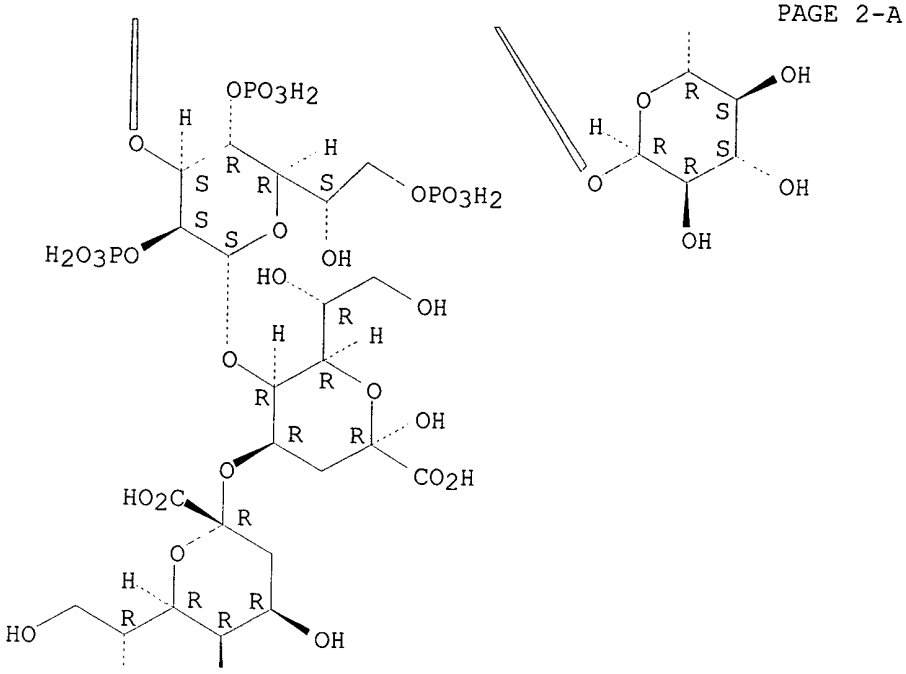

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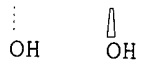
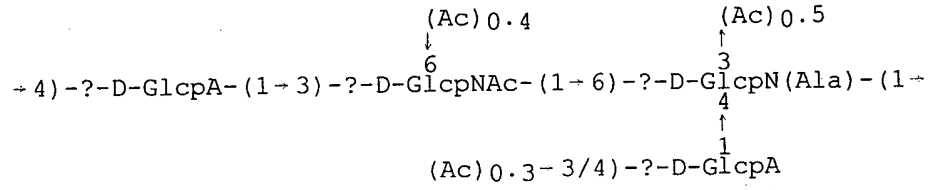


REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:185353 CAPLUS
DOCUMENT NUMBER: 126:293542
TITLE: Structure of the O-specific polysaccharide of Proteus penneri strain 25 containing N-(L-alanyl) and multiple O-acetyl groups in a tetrasaccharide repeating unit
AUTHOR(S): Arbatsky, Nikolay P.; Shashkov, Alexander S.; Widmalm, Goeran; Knirel, Yuriy A.; Zych, Krystyna; Sidorczyk, Zygmunt
CORPORATE SOURCE: Arrhenius Laboratory, Stockholm University, Stockholm, S-106 91, Swed.
SOURCE: Carbohydr. Res. (1997), 298(3), 229-235
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



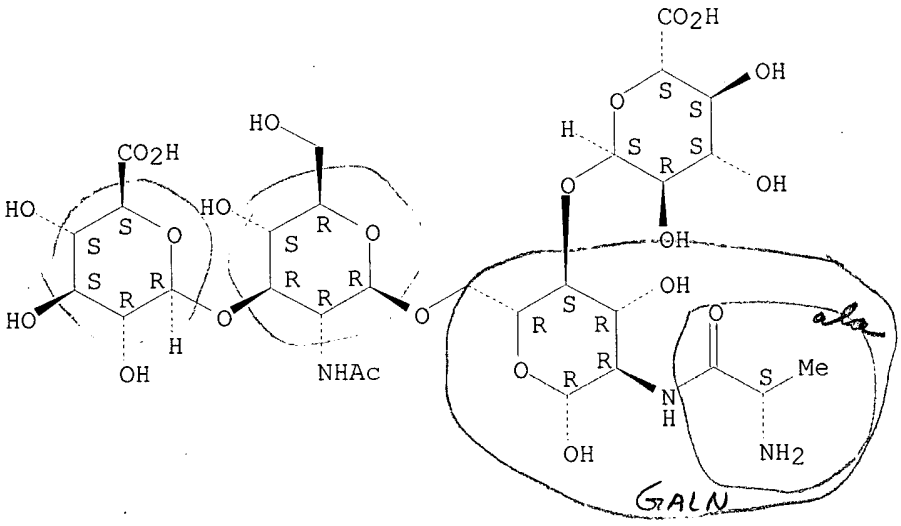
AB Mol. structure of the oligosaccharide I repeating unit of polysaccharide, isolated from Proteus penneri, has been investigated. Based on sugar and methylation analyses, O-deacetylation, Smith degrdn., and 1H and 13C NMR spectroscopy, including 2D COSY, 1H-detected 1H, 13C heteronuclear single-quantum coherence (HSQC), and 1H-detected 1H, 13C heteronuclear multiple-bond connectivity (HMBC) expts., the following structure of the O-specific polysaccharide of Proteus penneri strain 25 was established where D-GlcN(L-Ala) is 2-(L-alanylamido)-2-deoxy-D-glucose.

IT **189043-62-7DP**, partially acetylated
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (mol. structure of O-specific polysaccharide of Proteus penneri strain 25 contg. N-(L-alanyl) and multiple O-acetyl groups in a tetrasaccharide repeating unit)

RN 189043-62-7 CAPLUS

CN .beta.-D-Glucopyranose, O-.alpha.-D-glucopyranuronosyl-(1.fwdarw.4)-O-[O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.6)]-2-[[(2S)-2-amino-1-oxopropyl]amino]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L28 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:203373 CAPLUS

DOCUMENT NUMBER: 124:255405

TITLE: Structure of a decasaccharide isolated by mild acid degradation and dephosphorylation of the lipopolysaccharide of Pseudomonas fluorescens strain ATCC 49271

AUTHOR(S): Knirel, Yuriy A.; Helbig, Juergen H.; Zaehringer, Ulrich

CORPORATE SOURCE: Forschungszentrum Borstel, Zentrum Medizin Biowissenschaften, Borstel, 23845, Germany

Searched by Barb O'Bryen STIC 308-4291

SOURCE: Carbohydr. Res. (1996), 283, 129-39
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English

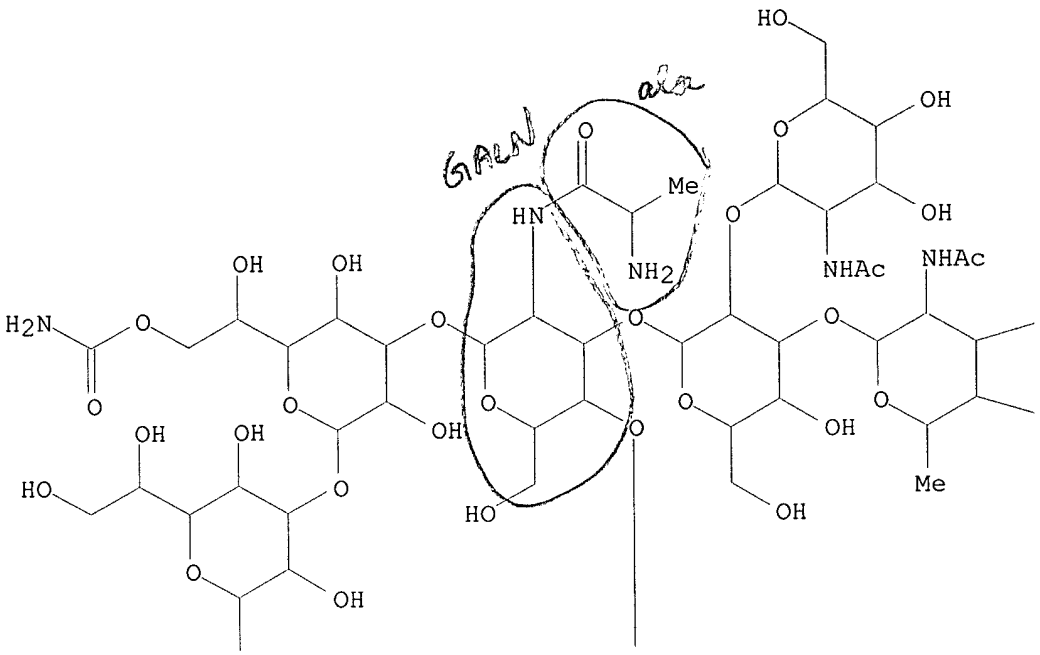
AB Mild acid degrdn. of the Pseudomonas fluorescens strain ATCC 49271 lipopolysaccharide resulted in a core oligosaccharide contg. D-glucose, 2-acetamido-2-deoxy-D-glucose, 2-(L-alanylamino)-2-deoxy-D-galactose, 2-acetamido-2,6-dideoxy-D-glucose (QuiNAc), 2-acetamido-2,6-dideoxy-L-galactose (FucNAc), L-glycero-D-manno-heptose (Hep), 3-deoxy-D-manno-octulosonic acid (Kdo, present in multiple forms), and 5-acetamidino-7-acetamido-3,5,7,9-tetradeoxy-L-glycero-D-galacto-nonulosonic acid (a di-N-acyl deriv. of legionaminic acid, Non) as well as O-acetyl, O-carbamoyl, and phosphate groups, including triphosphate groups. The dephosphorylated (HF) decasaccharide and products of its partial and full O-deacylation were studied by methylation anal., GLC-MS, and 1H NMR spectroscopy, including 1D NOE and 2D shift-correlated spectroscopy (COSY). The core oligosaccharide of P. fluorescens strain ATCC 49271 was found to be a decasaccharide (with a partially degraded Kdo region) and one O-antigen repeating unit (di-N-acyllegionaminic acid, Non) attached. The structure of the dephosphorylated core oligosaccharide is reported.

IT **175361-46-3D**, phosphorylated
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(structure of core decasaccharide and attached O antigen from lipopolysaccharide of Pseudomonas fluorescens)

RN 175361-46-3 CAPLUS

CN .alpha.-D-manno-2-Octulopyranosonic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.2)-O-[O-7-(acetylamino)-3,5,7,9-tetradeoxy-5-[(1-iminoethyl)amino]-L-glycero-.alpha.-D-galacto-2-nonulopyranosonosyl-(2.fwdarw.4)-O-3-O-acetyl-2-(acetylamino)-2,6-dideoxy-.alpha.-L-galactopyranosyl-(1.fwdarw.3)-2-(acetylamino)-2,6-dideoxy-.beta.-D-glucopyranosyl-(1.fwdarw.3)]-O-.beta.-D-glucopyranosyl-(1.fwdarw.3)-O-[6-O-acetyl-.alpha.-D-glucopyranosyl-(1.fwdarw.4)]-O-(S)-2-[(2-amino-1-oxopropyl)amino]-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.3)-O-7-O-(aminocarbonyl)-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.3)-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.5)-3-deoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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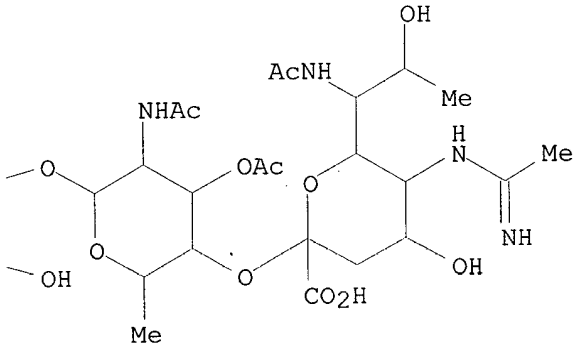

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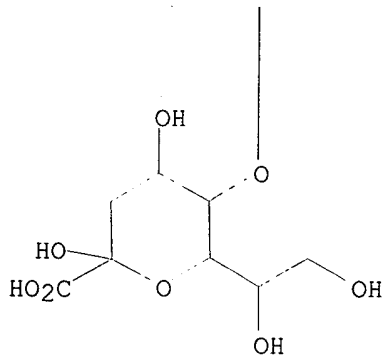
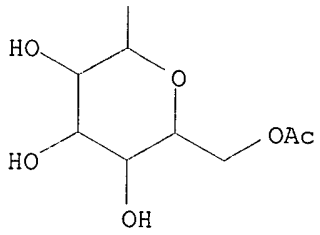
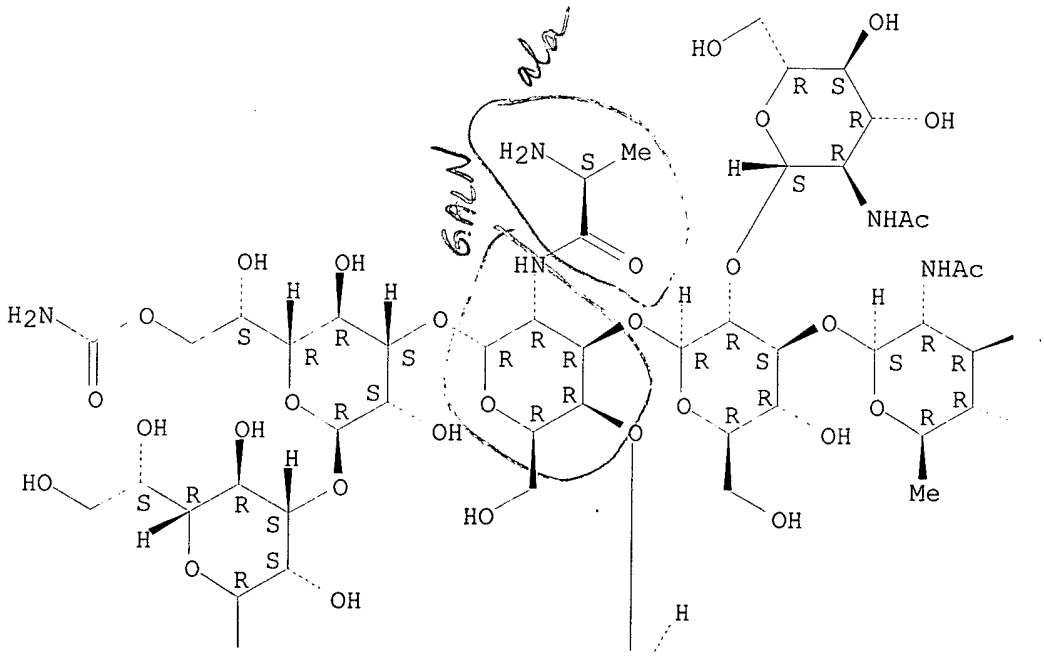




IT **175361-47-4D**, phosphorylated
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(structure of core decasaccharide from lipopolysaccharide of Pseudomonas fluorescens)
RN 175361-47-4 CAPLUS
CN .alpha.-D-manno-2-Octulopyranosonic acid, O-3-O-acetyl-2-(acetylamino)-2,6-dideoxy-.alpha.-L-galactopyranosyl-(1.fwdarw.3)-O-2-(acetylamino)-2,6-dideoxy-.beta.-D-glucopyranosyl-(1.fwdarw.3)-O-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl(1.fwdarw.2)]-O-.beta.-D-glucopyranosyl-(1.fwdarw.3)-O-[6-O-acetyl-.alpha.-D-glucopyranosyl-(1.fwdarw.4)]-O-(S)-2-[(2-amino-1-oxopropyl)amino]-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.3)-O-7-O-(aminocarbonyl)-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.3)-O-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.5)-O-[3-deoxy-.alpha.-D-manno-2-octulopyranosonosyl-(2.fwdarw.4)]-3-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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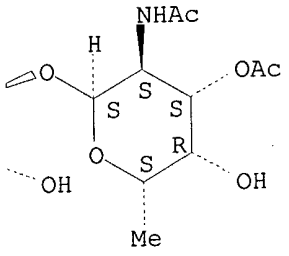

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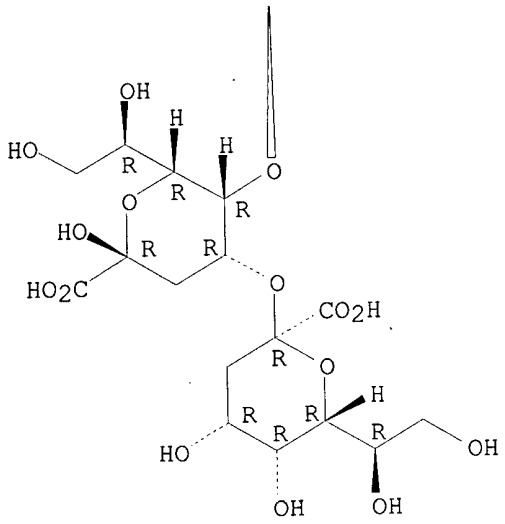
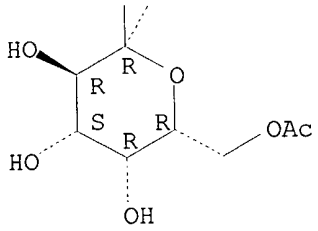




L28 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:956852 CAPLUS

DOCUMENT NUMBER: 124:4610

TITLE: Structural elucidation of the lipopolysaccharide core region of the O-chain-deficient mutant strain A28 from Pseudomonas aeruginosa serotype 06 (International Antigenic Typing Scheme)

AUTHOR(S): Masoud, Hussein; Sadovskaya, Irina; de Kievit, Teresa; Altman, Eleonora; Richards, James C.; Lam, Joseph S.

CORPORATE SOURCE: Inst. Biological Sciences, National Research Council Canada, Ottawa, ON, K1A 0R6, Can.

SOURCE: J. Bacteriol. (1995), 177(23), 6718-26
CODEN: JOBAAY; ISSN: 0021-9193

DOCUMENT TYPE: Journal

LANGUAGE: English

Searched by Barb O'Bryen STIC 308-4291

AB The lipopolysaccharide (LPS) of the P. aeruginosa serotype 06 rough-type mutant A28 was isolated by a modified PhOH-CHCl3-petroleum ether extn. method. Deoxycholate-PAGE indicated a single band with mobility similar to that of the complete core region of the wild-type parent serotype 06 (International Antigenic Typing Scheme) strain. Compositional anal. of the LPS indicated that the core oligosaccharide was composed of D-glucose (3 units), L-rhamnose (1 unit), 2-amino-2-deoxy-D-galactose (1 unit), L-glycero-D-mannoheptose (2 units), 3-deoxy-D-mannooctulosonic acid (2 units), L-alanine (1 unit), and phosphate (2 units). Under the mild conditions of hydrolysis with methanolic HCl, a 7-O-carbamoyl substituent was obsd. on the 2nd heptose residue. The glycan structure of the LPS was detd. by employing 1- and 2-dimensional NMR spectroscopy and mass spectrometry-based methods with a backbone oligosaccharide that was obtained from the LPS by deacylation, dephosphorylation, and redn. of the terminal glucosamine. On the basis of the results of the present study and earlier work with the P. aeruginosa 06-derived core-defective mutant R5, a structural model for the complete core oligosaccharide is proposed.

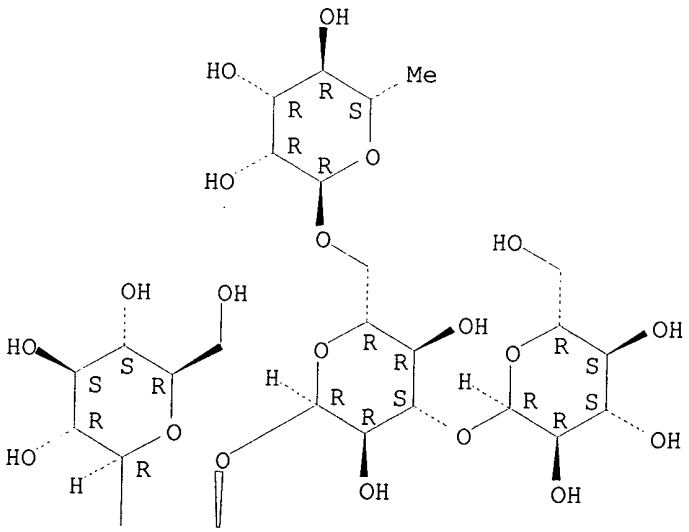
IT **171422-54-1**
RL: PRP (Properties)
(structure of the lipopolysaccharide core region of the O-chain-deficient mutant strain A28 from Pseudomonas aeruginosa serotype 06)

RN 171422-54-1 CAPLUS

CN .alpha.-D-manno-2-Octulopyranosonic acid, O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.6)-O-[.alpha.-D-glucopyranosyl-(1.fwdarw.3)]-O-.alpha.-D-glucopyranosyl-(1.fwdarw.4)-O-[.beta.-D-glucopyranosyl-(1.fwdarw.3)]-O-2-[(2-amino-1-oxopropyl)amino]-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.3)-O-7-O-(aminocarbonyl)-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.3)-O-2,4-di-O-phosphono-L-glycero-.alpha.-D-manno-heptopyranosyl-(1.fwdarw.5)-O-3-deoxy-.alpha.-D-manno-2-octulopyranosonosyl-(2.fwdarw.4)-3-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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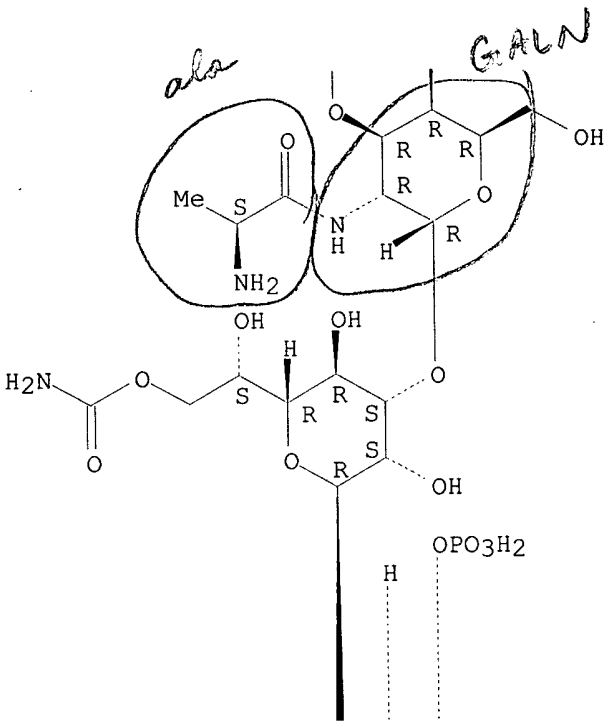

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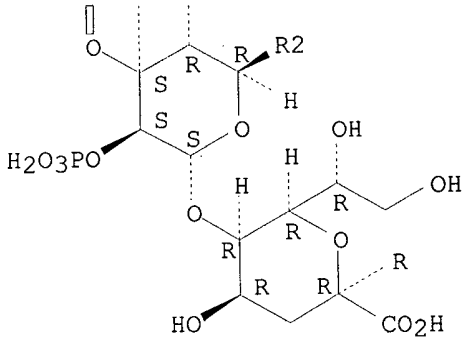

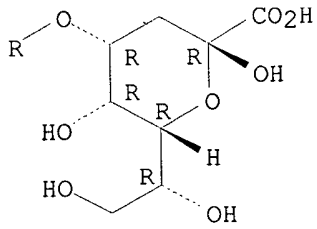

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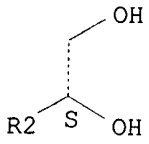

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HIGHEST GRANTED PATENT NUMBER: US6357047
HIGHEST APPLICATION PUBLICATION NUMBER: US2002032920
CA INDEXING IS CURRENT THROUGH 14 Mar 2002 (20020314/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 14 Mar 2002 (20020314/PD)
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FILE COVERS 1907 - 18 Mar 2002  VOL 136 ISS 12
FILE LAST UPDATED: 15 Mar 2002  (20020315/ED)

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and 1/23/02.  As of 1/23/02, the situation has been resolved.  Searches
and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry
Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
be incomplete.  See the NEWS message on this topic for more information.


L31        14313 SEA FILE=CAPLUS ABB=ON  PSEUDOMONAS AERUGINOSA+NT/CT
L32        19275 SEA FILE=CAPLUS ABB=ON  LIPOPOLYSACCHARIDES/CT
L33         2957 SEA FILE=CAPLUS ABB=ON  CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTAN
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L34            5 SEA FILE=CAPLUS ABB=ON  L31 AND L32 AND L33


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 FILE LAST UPDATED: 17 MAR 2002 (20020317/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

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Basic Index. See HELP SFIELDS for details.

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FILE COVERS 1974 TO 14 Mar 2002 (20020314/ED)

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L43        25002 SEA FILE=EMBASE ABB=ON  LIPOPOLYSACCHARIDE+NT/CT
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HIGHEST APPLICATION PUBLICATION NUMBER: US2002032920
CA INDEXING IS CURRENT THROUGH 14 Mar 2002 (20020314/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 14 Mar 2002 (20020314/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2001
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2001

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L54 492 SEA FILE=USPATFULL ABB=ON ((PSEUDOMONAS/CLM,AB,TI OR PS/CLM,AB,TI)(W) AERUGINOSA/CLM,AB,TI)
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L45      112624 SEA (PSEUDOMONAS OR PS)(W) AERUGINOSA
L46      142808 SEA LIPOPOLYSACCHARIDE# OR (LIPOPOLY OR LIPO POLY)(W) SACCHARID
                E# OR LIPO POLYSACCHARIDE#
L47       14017 SEA CYSTIC FIBROSIS (W)(TRANSMEMBRANE OR TRANS MEMBRANE) (W)
                CONDUCTANCE REGULATOR# OR CFTR#
L48          48 SEA L45 AND L46 AND L47


=> dup rem 139,134,148,144,155
FILE 'MEDLINE' ENTERED AT 12:26:43 ON 18 MAR 2002

FILE 'CAPLUS' ENTERED AT 12:26:43 ON 18 MAR 2002
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PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L48
PROCESSING COMPLETED FOR L44
PROCESSING COMPLETED FOR L55
L57           25 DUP REM L39 L34 L48 L44 L55 (40 DUPLICATES REMOVED)
                 ANSWERS '1-6' FROM FILE MEDLINE
                 ANSWERS '7-9' FROM FILE CAPLUS
                 ANSWERS '10-12' FROM FILE PASCAL
                 ANSWERS '13-17' FROM FILE BIOSIS
                 ANSWER '18' FROM FILE BIOTECHNO
                 ANSWERS '19-20' FROM FILE ESBIOBASE
                 ANSWERS '21-24' FROM FILE SCISEARCH
                 ANSWER '25' FROM FILE USPATFULL

=> d ibib ab 1-25; fil hom
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L57 ANSWER 1 OF 25 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001296660 MEDLINE
DOCUMENT NUMBER: 21276424 PubMed ID: 11278360
TITLE: Cystic fibrosis pathogens activate Ca2+-dependent mitogen-activated protein kinase signaling pathways in airway epithelial cells.
AUTHOR: Ratner A J; Bryan R; Weber A; Nguyen S; Barnes D; Pitt A; Gelber S; Cheung A; Prince A
CORPORATE SOURCE: College of Physicians & Surgeons, Columbia University, New York, New York 10032, USA.
CONTRACT NUMBER: HL56194 (NHLBI)
HL60293 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jun 1) 276 (22) 19267-75.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB Much of the pulmonary disease in cystic fibrosis is associated with polymorphonuclear leukocyte-dominated airway inflammation caused by bacterial infection. Respiratory epithelial cells express the polymorphonuclear chemokine interleukin-8 (IL-8) in response to ligation of asialylated glycolipid receptors, which are increased on damaged or regenerating cells and those with **cystic fibrosis transmembrane conductance regulator** mutations. Because both Pseudomonas aeruginosa and Staphylococcus aureus, the most common pathogens in cystic fibrosis, bind asialylated glycolipid receptors such as asialoGM1, we postulated that diverse bacteria can activate a common epithelial signaling pathway to elicit IL-8 expression. P. aeruginosa PAO1 but not pil mutants and S. aureus RN6390 but not the agr mutant RN6911 stimulated increases in [Ca(2+)](i) in 1HAEo- airway epithelial cells. This response stimulated p38 and ERK1/2 mitogen-activated protein kinase (MAPK) signaling cascades resulting in NF-kappaB activation and IL-8 expression. Ligation of the asialoGM1 receptor or thapsigargin-elicited Ca(2+) release activated this pathway, whereas P. aeruginosa lipopolysaccharide did not. The rapid kinetics of epithelial activation precluded bacterial invasion of the epithelium. Recognition of asialylated glycolipid receptors on airway epithelial cells provides a common pathway for Gram-positive and Gram-negative organisms to initiate an epithelial inflammatory response.

L57 ANSWER 2 OF 25 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001677591 MEDLINE
DOCUMENT NUMBER: 21552978 PubMed ID: 11696036
TITLE: Epithelial cell contact-induced alterations in Salmonella enterica serovar Typhi lipopolysaccharide are critical for bacterial internalization.
AUTHOR: Lyczak J B; Zaidi T S; Grout M; Bittner M; Contreras I; Pier G B
CORPORATE SOURCE: The Channing Laboratory, Brigham and Women's Hospital, 181 Longwood Avenue, Boston, MA 02115, USA..
jlyczak@channing.harvard.edu
CONTRACT NUMBER: AI 22535 (NIAID)
HL 58398 (NHLBI)
SOURCE: CELLULAR MICROBIOLOGY, (2001 Nov) 3 (11) 763-72.
Journal code: 100883691. ISSN: 1462-5814.
PUB. COUNTRY: England: United Kingdom

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011129
Last Updated on STN: 20020215
Entered Medline: 20020214

AB The invasion of Pseudomonas aeruginosa and Salmonella enterica serovar Typhi into epithelial cells depends on the **cystic fibrosis transmembrane conductance regulator** (**CFTR**) protein as an epithelial receptor. In the case of P. aeruginosa, the bacterial ligand for **CFTR** is the outer core oligosaccharide portion of the lipopolysaccharide (LPS). To determine whether serovar Typhi LPS is also a bacterial ligand mediating internalization, we used both P. aeruginosa and serovar Typhi LPS as a competitive inhibitor of serovar Typhi invasion into the epithelial cell line T84. P. aeruginosa LPS containing a complete core efficiently inhibited serovar Typhi invasion. However, neither killed wild-type Typhi cells nor purified LPS were effective inhibitors. LPS from mutant Typhi strains defective in O side-chain synthesis, but with an apparently normal core, was capable of inhibiting invasion, but LPS obtained from a deeper rough mutant strain with alterations in fast-migrating core oligosaccharide failed to inhibit invasion. Lastly, exposure of wild-type serovar Typhi to T84 cultures before heat killing resulted in a structural alteration in its LPS that allowed the heat-killed cells to inhibit invasion of wild-type serovar Typhi. These data indicate that the serovar Typhi LPS core, like the P. aeruginosa LPS core, is a ligand mediating internalization of bacteria by epithelial cells, and that exposure of this ligand on wild-type Typhi is induced by the bacteria's interaction with host cells.

L57 ANSWER 3 OF 25 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999364934 MEDLINE
DOCUMENT NUMBER: 99364934 PubMed ID: 10433940
TITLE: Genistein inhibits constitutive and inducible NFkappaB activation and decreases IL-8 production by human cystic fibrosis bronchial gland cells.
AUTHOR: Tabary O; Escotte S; Couetil J P; Hubert D; Dusser D; Puchelle E; Jacquot J
CORPORATE SOURCE: INSERM Unite 514,(*) Reims Hopital Broussais, Paris Hopital Cochin, Paris, France.
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1999 Aug) 155 (2) 473-81. Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990831

AB The inflammatory pathogenesis in airways of patients with cystic fibrosis (CF) is still unresolved. We demonstrate here that in in situ human DeltaF508 homozygous CF bronchial tissues, submucosal gland cells exhibit an absence of inhibitor factor kappaBalpha (IkappaBalpha) and high levels of chemokine interleukin-8 (IL-8) expression. These results were confirmed by cultured human CF bronchial gland cells in which a lack of cytosolic IkappaBalpha and high levels of constitutively activated nuclear factor kappaB (NFkappaB) associated with an up-regulation of IL-8 production (13-fold increase) were found when compared to non-CF (control) disease bronchial gland cells. We also demonstrated that the isoflavone genistein, a well known **CFTR** mutant Cl(-) channel stimulator, significantly reduces the endogenous and Pseudomonas aeruginosa lipopolysaccharide-

induced IL-8 production in cultured CF bronchial gland cells by increasing cytosolic IkappaBalpha protein levels. Overall, results show that genistein is a potent inhibitor of the activated NFkappaB identified in CF gland cells. This strong inhibition of constitutively activated NFkappaB and the resulting down-regulation of IL-8 production by genistein in the CF gland cells highlights the key role played by cytosolic IkappaBalpha in the regulation of inflammatory processes in CF human airway cells.

L57 ANSWER 4 OF 25 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 97175711 MEDLINE
DOCUMENT NUMBER: 97175711 PubMed ID: 9023366
TITLE: Transcriptional activation of mucin by Pseudomonas aeruginosa lipopolysaccharide in the pathogenesis of cystic fibrosis lung disease.
AUTHOR: Li J D; Dohrman A F; Gallup M; Miyata S; Gum J R; Kim Y S; Nadel J A; Prince A; Basbaum C B
CORPORATE SOURCE: Department of Anatomy, Cardiovascular Research Institute, University of California, San Francisco 94143, USA.
CONTRACT NUMBER: HL 24136 (NHLBI)
HL 43762 (NHLBI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Feb 4) 94 (3) 967-72.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U67167
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19990129
Entered Medline: 19970310

AB An unresolved question in cystic fibrosis (CF) research is how mutations of the CF transmembrane conductance regulator, a Cl ion channel, cause airway mucus obstruction leading to fatal lung disease. Recent evidence has linked the CF transmembrane conductance regulator mutation to the onset and persistence of Pseudomonas aeruginosa infection in the airways, and here we provide evidence directly linking P. aeruginosa infection to mucus overproduction. We show that P. aeruginosa lipopolysaccharide profoundly upregulates transcription of the mucin gene MUC 2 in epithelial cells via inducible enhancer elements and that this effect is blocked by the tyrosine kinase inhibitors genistein and tyr-phostin AG 126. These findings improve our understanding of CF pathogenesis and suggest that the attenuation of mucin production by lipopolysaccharide antagonists and tyrosine kinase inhibitors could reduce morbidity and mortality in this disease.

L57 ANSWER 5 OF 25 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998086347 MEDLINE
DOCUMENT NUMBER: 98086347 PubMed ID: 9425267
TITLE: Pseudomonas aeruginosa lipopolysaccharide induces CF-like alteration of protein secretion by human tracheal gland cells.
AUTHOR: Kammouni W; Figarella C; Baeza N; Marchand S; Merten M D
CORPORATE SOURCE: Groupe de Recherche sur les Glandes Exocrines, Faculte de medecine, Marseille, France.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Dec 18) 241 (2) 305-11.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126

AB Human tracheal gland (HTG) serous cells are now believed to play a major role in the physiopathology of cystic fibrosis. Because of the persistent inflammation and the specific infection by Pseudomonas aeruginosa in the lung, we looked for the action of the lipopolysaccharide (LPS) of this bacteria on human tracheal gland cells in culture by studying the secretion of the secretory leukocyte proteinase inhibitor (SLPI) which is a specific serous secretory marker of these cells. Treatment with Pseudomonas aeruginosa LPS resulted in a significant dose-dependent increase in the basal production of SLPI (+ 250 +/- 25%) whilst the SLPI transcript mRNA levels remained unchanged. This LPS-induced increase in secretion was inhibited by glucocorticoides. Furthermore, LPS treatment of HTG cells induces a loss of responsiveness to carbachol and isoproterenol but not to adenosine triphosphate. These findings indicate that HTG cells treated by Pseudomonas aeruginosa LPS have the same behavior as those previously observed with CF-HTG cells. Exploration by using reverse transcriptase polymerase chain reaction amplification showed that LPS downregulated **cystic fibrosis transmembrane conductance regulator** (**CFTR**) mRNA expression in HTG cells indicative of a link between **CFTR** function and consequent CF-like alteration in protein secretory process.

L57 ANSWER 6 OF 25 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 96138427 MEDLINE
DOCUMENT NUMBER: 96138427 PubMed ID: 8539601
TITLE: Role of mutant **CFTR** in hypersusceptibility of cystic fibrosis patients to lung infections.
AUTHOR: Pier G B; Grout M; Zaidi T S; Olsen J C; Johnson L G; Yankaskas J R; Goldberg J B
CORPORATE SOURCE: Channing Laboratory, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115-5899, USA.
CONTRACT NUMBER: AI22806 (NIAID)
AI35674 (NIAID)
HL42384 (NHLBI)
SOURCE: SCIENCE, (1996 Jan 5) 271 (5245) 64-7.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960221
Last Updated on STN: 19960221
Entered Medline: 19960208

AB Cystic fibrosis (CF) patients are hypersusceptible to chronic Pseudomonas aeruginosa lung infections. Cultured human airway epithelial cells expressing the delta F508 allele of the **cystic fibrosis transmembrane conductance regulator** (**CFTR**) were defective in uptake of P. aeruginosa compared with cells expressing the wild-type allele. Pseudomonas aeruginosa lipopolysaccharide (LPS)-core oligosaccharide was identified as the bacterial ligand for epithelial cell ingestion; exogenous oligosaccharide inhibited bacterial ingestion in a neonatal mouse model, resulting in increased amounts of bacteria in the lungs. **CFTR** may contribute to a host-defense mechanism that is important for clearance of P. aeruginosa from the respiratory tract.

L57 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:427380 CAPLUS
DOCUMENT NUMBER: 135:51028

TITLE: Methods and products for treating Pseudomonas infection
INVENTOR(S): Pier, Gerald B.
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6245735	B1	20010612	US 1996-681838	19960729

AB Methods and products for up-regulating **cystic fibrosis transmembrane conductance regulators** are provided, including methods and products for the treatment of P. aeruginosa infection. The products include polysaccharides that interact with the **cystic fibrosis transmembrane conductance regulator** (**CFTR**). The polysaccharide compns. of the invention may be administered to a subject in order to enhance the uptake of P. aeruginosa into the epithelial cells of the subject. The invention also encompasses compns. comprising a lipopolysaccharide-binding region of a **CFTR** linked to an anti-Pseudomonal drug and methods of use of such compns. Compns. and methods for gene therapy are also disclosed. The compns. include polysaccharides that bind to **CFTR** coupled to a gene delivery vehicle.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 2000:700256 CAPLUS
DOCUMENT NUMBER: 133:361459
TITLE: Pseudomonas aeruginosa induction of apoptosis in respiratory epithelial cells. Analysis of the effects of **cystic fibrosis transmembrane conductance regulator** dysfunction and bacterial virulence factors
AUTHOR(S): Rajan, Sujatha; Cacalano, Grace; Bryan, Ruth; Ratner, Adam J.; Sontich, Claudia U.; Van Heerckeren, Anna; Davis, Pamela; Prince, Alice
CORPORATE SOURCE: Department of Pediatric Infectious Diseases, College of Physicians & Surgeons, Columbia University, New York, NY, 10032, USA
SOURCE: Am. J. Respir. Cell Mol. Biol. (2000), 23(3), 304-312
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Thoracic Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Airway epithelial cells can respond to infection by activating several signaling pathways. We examd. the induction of apoptosis in response to Pseudomonas aeruginosa PAO1 in normal cells and several cystic fibrosis (CF) and cor. cell lines. Epithelial cells in monolayers with tight junctions, confirmed by apical ZO-1 staining demonstrated by confocal microscopy, were entirely resistant to PAO1-induced apoptosis. In contrast, cell lines such as 9HTEo- cells that do not form tight junctions were susceptible, with 50% of the population apoptotic after 6 h of exposure to PAO1. CF transmembrane conductance regulator (**CFTR**) dysfunction caused by different mechanisms (trafficking mutations, overexpression of the regulatory domain or antisense constructs) did not alter rates of apoptosis, nor were differences apparent in terminal

deoxyribonucleotidyl transferase-mediated deoxyuridine triphosphate-biotin nick-end labeling detection of apoptotic airway cells from PAO1 infected **cftr** -/- or control mice. Bacterial expression of specific adhesins, complete lipopolysaccharide, and a functional type III secretion system were all necessary to evoke apoptosis even in susceptible epithelial cells. Unlike other mucosal surfaces, the airway epithelium is highly resistant to apoptosis, and this response is activated only when the appropriate epithelial conditions are present as well as fully virulent P. aeruginosa capable of coordinately expressing both adhesins and cytotoxins.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:521434 CAPLUS
DOCUMENT NUMBER: 131:139488
TITLE: Bactericidal factor in human airway surface fluid and uses thereof
INVENTOR(S): Welsh, Michael J.; Smith, Jeffrey J.; Travis, Sue M.; Greenberg, Everett P.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA
SOURCE: U.S., 35 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5939393	A	19990817	US 1997-840876	19970417
PRIORITY APPLN. INFO.:			US 1997-41601P P	19970325

AB A bactericidal factor isolated from the surface fluid of airway epithelial cells and uses therefore is described. The bactericidal factor is characterized as having the following features: (a) a mol. wt. of less than 10 kd; (b) heat stable; (c) broad spectrum activity including gram pos. and gram neg. bacteria, fungi, and methicillin-resistant Staphylococcus; and (d) decreased antimicrobial activity in increasing salt concn. The factor is a defensin-like mol. In cystic fibrosis (CF) patients which have abnormal levels of salt concn. in the airways due to defective Cl- transport, the factor is inactivated. leading for the first time to the explanation of the pulmonary infection assocd. with CF.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 10 OF 25 PASCAL COPYRIGHT 2002 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 1997-0021092 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1997 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): How mutant **CFTR** may contribute to **Pseudomonas aeruginosa** infection in cystic fibrosis
Interactions of bacteria with airway cells and secretions
AUTHOR: PIER G. B.; GROUT M.; ZAIDI T. S.; GOLDBERG J. B.
CORPORATE SOURCE: Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States
SOURCE: American journal of respiratory and critical care medicine, (1996), 154(4, p.2), S175-S182, 35 refs.
Conference: 11 Transatlantic Airway Conference, Lucerne (Switzerland), 11 Jan 1996
ISSN: 1073-449X

DOCUMENT TYPE: Journal; Conference
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-2013, 354000066664330080

AB Patients with cystic fibrosis (CF) have a pronounced hypersusceptibility (80 to 90%) to **Pseudomonas aeruginosa** infection. We hypothesized that airway epithelial cell ingestion of bacteria followed by cellular desquamation may protect the lung from infection, and epithelial cells expressing mutant forms of the **cystic fibrosis transmembrane conductance regulator** (**CFTR**) may be defective in this function. We found that transformed human airway epithelial cells homozygous for the AFS08 allele of **CFTR** were significantly defective in uptake of P. aeruginosa compared with the same cell line complemented with the wild-type allele of **CFTR**. Partial membrane expression of the AF508 **CFTR** protein occurs in cells grown at 26.degree.C, and under these conditions uptake of P. aeruginosa occurred at levels comparable to cells with a wild-type allele of **CFTR**. Epithelial cell ingestion assays using isogenic bacterial strains differing in **lipopolysaccharide** (LPS) phenotype, along with inhibition studies, identified the LPS-core oligosaccharide as the bacterial ligand for epithelial cell invasion. Inhibition of epithelial cell ingestion of P. aeruginosa in a neonatal mouse lung infection model led to increased levels of bacteria in the lungs 24 and 48 h after infection. Defective epithelial cell internalization of P. aeruginosa may be a critical factor in hypersusceptibility of CF patients to chronic lung infections.

L57 ANSWER 11 OF 25 PASCAL COPYRIGHT 2002 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 1995-0169694 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Serum IgG response to Burkholderia cepacia outer membrane antigens in cystic fibrosis : assessment of cross-reactivity with **Pseudomonas aeruginosa**
AUTHOR: LACY D. E.; SMITH A. W.; STABLEFORTH D. E.; SMITH G.; WELLER P. H.; BROWN M. R. W.
CORPORATE SOURCE: Royal Liverpool children's NHS Trust, Liverpool, United Kingdom
SOURCE: FEMS immunol. med. microbiol., (1995), 10(3-4), 253-261, 31 refs.
ISSN: 0928-8244
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Netherlands
LANGUAGE: English
AVAILABILITY: INIST-17567B, 354000059688550110

AB Burkholderta cepacia (Pseudomonas cepacia) is now recognised as an important pathogen in cystic fibrosis patients several reports have suggested that sputum-culture-proven colonisation occurs despite the presence of specific antibody. In an attempt to establish the use of antibody studies as diagnostic and prognostic indicators of B. cepacia infection, we have examined the IgG response to B. cepacia outer membrane proteins and **lipopolysaccharide** in patients also colonised with P. aeruginosa. The B. cepacia strains were grown in a modified iron-depleted chemically defined medium and outer membrane components examined by SDS-PAGE and immunoblotting. IgG antibodies were detected against B. cepacia outer membrane antigens, which were not diminished by extensive preadsorption with P. aeruginosa. The response to B. cepacia O-antigen could be readily removed by adsorption of serum either with B. cepacia whole cells or purified LPS, whereas we were unable to adsorb anti-outer membrane protein antibodies using B. cepacia whole cells. The

inability to adsorb anti-outer membrane protein antibodies using B. cepacia whole cells maybe due to non-exposed surface epitopes. Several B. cepacia sputum-culture negative patients colonised with P. aeruginosa had antibodies directed against B. cepacia outer membrane protein. This study suggests that there is a specific anti-B. cepacia LPS IgG response, which is not due to antibodies cross-reactive with P. aeruginosa. Our studies indicate that much of the B. cepacia anti-outer membrane protein response is specific and not attributable to reactivity against co-migrating LPS

L57 ANSWER 12 OF 25 PASCAL COPYRIGHT 2002 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 1995-0269657 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): **Lipopolysaccharide** (LPS), LPS-immune complexes and cytokines as inducers of pulmonary inflammation in patients with cystic fibrosis and chronic **Pseudomonas aeruginosa** lung infection
AUTHOR: KRONBORG GITTE
CORPORATE SOURCE: Rigshosp., dep. clin. microbiology and Danish CF cent., Copenhagen, Denmark
Kobenhavns universitet, Kobenhavn, Denmark (tutelle)
SOURCE: APMIS. Acta pathologica, microbiologica et immunologica scandinavica. Supplementum, (1995; 1995), 103(50), refs. 5 p.
30 p.
ISSN: 0903-465X
Dissertation Information: Kobenhavns universitet. Kobenhavn. DNK, Thesis
DOCUMENT TYPE: Journal; Dissertation
BIBLIOGRAPHIC LEVEL: Monographic
COUNTRY: Denmark
LANGUAGE: English
SUMMARY LANGUAGE: Danish
AVAILABILITY: INIST-948S, 354000056663500000

L57 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
ACCESSION NUMBER: 2000:438399 BIOSIS
DOCUMENT NUMBER: PREV200000438399
TITLE: Role of the **cystic fibrosis transmembrane conductance regulator** in innate immunity to **Pseudomonas aeruginosa** infections.
AUTHOR(S): Pier, Gerald B. (1)
CORPORATE SOURCE: (1) Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115-5899 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (August 1, 2000) Vol. 97, No. 16, pp. 8822-8828. print.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Chronic **Pseudomonas aeruginosa** infection occurs in 75-90% of patients with cystic fibrosis (CF). It is the foremost factor in pulmonary function decline and early mortality. A connection has been made between mutant or missing CF transmembrane conductance regulator (**CFTR**) in lung epithelial cell membranes and a failure in innate immunity leading to initiation of P. aeruginosa infection. Epithelial cells use **CFTR** as a receptor for internalization of P. aeruginosa via endocytosis and subsequent removal of bacteria from the

airway. In the absence of functional **CFTR**, this interaction does not occur, allowing for increased bacterial loads in the lungs. Binding occurs between the outer core of the bacterial **lipopolysaccharide** and amino acids 108-117 in the first predicted extracellular domain of **CFTR**. In experimentally infected mice, inhibiting **CFTR** -mediated endocytosis of P. aeruginosa by inclusion in the bacterial inoculum of either free bacterial **lipopolysaccharide** or **CFTR** peptide 108-117 resulted in increased bacterial counts in the lungs. **CFTR** is also a receptor on gastrointestinal epithelial cells for Salmonella enterica serovar Typhi, the etiologic agent of typhoid fever. There was a significant decrease in translocation of this organism to the gastrointestinal submucosa in transgenic mice that are heterozygous carriers of a mutant DELTAF508 **CFTR** allele, suggesting heterozygous **CFTR** carriers may have increased resistance to typhoid fever. The identification of **CFTR** as a receptor for bacterial pathogens could underlie the biology of CF lung disease and be the basis for the heterozygote advantage for carriers of mutant alleles of **CFTR**.

L57 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
ACCESSION NUMBER: 1996:539230 BIOSIS
DOCUMENT NUMBER: PREV199699261586
TITLE: How mutant **CFTR** may contribute to **Pseudomonas aeruginosa** infection in cystic fibrosis.
AUTHOR(S): Pier, Gerald B. (1); Grout, Martha; Zaidi, Tanweer S.; Goldberg, Joanna B.
CORPORATE SOURCE: (1) Channing Lab., 181 Longwood Ave., Boston, MA 02115-5899 USA
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996) Vol. 154, No. 4 PART 2, pp. S175-S182. ISSN: 1073-449X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Patients with cystic fibrosis (CF) have a pronounced hypersusceptibility (80 to 90%) to **Pseudomonas aeruginosa** infection. We hypothesized that airway epithelial cell ingestion of bacteria followed by cellular desquamation may protect the lung from infection, and epithelial cells expressing mutant forms of the **cystic fibrosis transmembrane conductance regulator** (**CFTR**) may be defective in this function. We found that transformed human airway epithelial cells homozygous for the DELTA-F508 allele of **CFTR** were significantly defective in uptake of P. aeruginosa compared with the same cell line complemented with the wild-type allele of **CFTR**. Partial membrane expression of the DELTA-F508 **CFTR** protein occurs in cells grown at 26 degree C, and under these conditions uptake of P. aeruginosa occurred at levels comparable to cells with a wild-type allele of **CFTR**. Epithelial cell ingestion assays using isogenic bacterial strains differing in **lipopolysaccharide** (LPS) phenotype, along with inhibition studies, identified the LPS-core oligosaccharide as the bacterial ligand for epithelial cell invasion. Inhibition of epithelial cell ingestion of P. aeruginosa in a neonatal mouse lung infection model led to increased levels of bacteria in the lungs 24 and 48 h after infection. Defective epithelial cell internalization of P. aeruginosa may be a critical factor in hypersusceptibility of CF patients to chronic lung infections.

L57 ANSWER 15 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:189002 BIOSIS
DOCUMENT NUMBER: PREV200200189002
TITLE: Interaction of the serovar Typhi LPS with its epithelial cell receptor, **CFTR**.

AUTHOR(S): Lyczak, J. B. (1); Zaidi, T. S. (1); Grout, M. (1); Bittner, W. M.; Contreras, I.; Pier, G. B. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, Boston, MA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 139. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print. Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001 ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The **cystic fibrosis transmembrane conductance regulator** (**CFTR**) protein mediates internalization of **Pseudomonas aeruginosa** and Salmonella enterica serovar Typhi into epithelial cells. This interaction may underlie serovar Typhi gastrointestinal (GI) translocation and innate immunity to P. aeruginosa lung infection. The ligand for **CFTR** is the LPS outer core oligosaccharide for P. aeruginosa, but is not known for serovar Typhi. To identify the serovar Typhi ligand we purified LPS from wild type and LPS mutant strains and used these to inhibit entry of serovar Typhi into T84 GI epithelial cells. While LPS from P. aeruginosa readily inhibited serovar Typhi entry into T84 cells, LPS from wild-type serovar Typhi cells did not. LPS from a serovar Typhi mutant strain with a complete core oligosaccharide but few O-side chains efficiently inhibited serovar Typhi cellular entry, while LPS isolated from another mutant lacking a complete core and O side chains did not inhibit entry. Importantly, after exposure of wild-type serovar Typhi to epithelial cells for 4 h there was a marked change in the LPS, revealed by SDS-PAGE, leading to a diminution of the O side chain. Thus, the ability of wild-type and mutant serovar Typhi to enter epithelial cells correlated with expression of LPS with a complete core oligosaccharide but few O-side chains. Further, serovar Typhi LPS and CPTR co-localized on epithelial cells, as shown by confocal microscopy of Texas Red labeled LPS and GFP-**CFTR** expressing MDCK cells. Finally, the increased cell-surface expression of **CFTR** protein by epithelial cells during infection with both P. aeruginosa and serovar Typhi was shown to be due to a redistribution of preexisting **CFTR** protein from cytoplasmic vesicles to the plasma membrane. Thus, wild-type serovar Typhi stimulates **CFTR** accumulation in the plasma membrane and modifies its LPS to acquire **CFTR**-binding ability to promote entry into GI epithelial cells.

L57 ANSWER 16 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:499653 BIOSIS
DOCUMENT NUMBER: PREV199900499653
TITLE: Pathogenicity of microbes associated with cystic fibrosis.
AUTHOR(S): Hutchison, Michael L. (1); Govan, John R.W. (1)
CORPORATE SOURCE: (1) Cystic Fibrosis Laboratory, Department of Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SOURCE: Microbes and Infection, (Oct., 1999) Vol. 1, No. 12, pp. 1005-1014. ISSN: 1286-4579.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cystic fibrosis patients are exceptionally prone to colonisation by a narrow spectrum of pathogenic bacteria. Since pulmonary infection presently, and for the foreseeable future, plays such a major role in CF lung disease, we review the microbes that are classically associated with CF and the virulence, inflammatory potential and resistance mechanisms which contribute to the reduction in life expectancy for colonised CF patients.

L57 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:69523 BIOSIS
DOCUMENT NUMBER: PREV200000069523
TITLE: The **cystic fibrosis transmembrane conductance regulator** (**CFTR**) regulates the sensitivity of macrophages to bacterial **lipopolysaccharide**.
AUTHOR(S): Hume, David (1); Thomas, Gordon (1); McMorran, Brendan (1); Ahadizadeh, Azita (1); McGlinn, Edwina (1); Lunn, Dominic (1); Lovelock, Paul (1); Delaney, Stephen (1); Costelloe, Elaine (1); Stacey, Katryn (1); Passey, Robert; Geczy, Carolyn; Wainwright, Brandon (1)
CORPORATE SOURCE: (1) Centre for Molecular and Cellular Biology, University of Queensland, Brisbane, QLD Australia
SOURCE: Journal of Endotoxin Research, (1999) Vol. 5, No. 3, pp. 177-178.
Meeting Info.: Fifth Conference of the International Endotoxin Society Santa Fe, New Mexico, USA September 12-15, 1998 The International Endotoxin Society . ISSN: 0968-0519.
DOCUMENT TYPE: Conference
LANGUAGE: English

L57 ANSWER 18 OF 25 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32525618 BIOTECHNO
TITLE: Transgenic cystic fibrosis mice exhibit reduced early clearance of **Pseudomonas aeruginosa** from the respiratory tract
AUTHOR: Schroeder T.H.; Reiniger N.; Meluleni G.; Grout M.; Coleman F.T.; Pier G.B.
CORPORATE SOURCE: Dr. G.B. Pier, Channing Laboratory, Department of Medicine, Harvard Medical School, 181 Longwood Avenue, Boston, MA 02115, United States.
E-mail: gpier@channing.harvard.edu
SOURCE: Journal of Immunology, (15 JUN 2001), 166/12 (7410-7418), 33 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The Cystic fibrosis (CF) transmembrane conductance regulator (**CFTR**) has been proposed to be an epithelial cell receptor for **Pseudomonas aeruginosa** involved in bacterial internalization and clearance from the lung. We evaluated the role of **CFTR** in clearing P. aeruginosa from the respiratory tract using transgenic CF mice that carried either the .delta.F508 **Cftr** allele or an allele with a **Cftr** stop codon (S489X). Intranasal application achieved P. aeruginosa lung infection in inbred C57BL/6 .delta.F508 **Cftr** mice, whereas .delta.F508 **Cftr** and S489X **Cftr** outbred mice required tracheal application of the inoculum to establish lung infection. CF mice showed significantly less ingestion of LPS-smooth P. aeruginosa by lung cells and significantly greater bacterial lung burdens 4.5 h postinfection than C57BL/6 wild-type mice. Microscopy of infected mouse and rhesus monkey tracheas clearly demonstrated ingestion of P. aeruginosa by epithelial cells in wild-type animals, mostly around injured areas of the epithelium. Desquamating cells loaded with P. aeruginosa could also be seen in these tissues. No difference was found between CF and wild-type mice challenged with an LPS-rough mucoid isolate of P. aeruginosa lacking the **CFTR** ligand. Thus, transgenic CF mice exhibit decreased clearance of P.

aeruginosa and increased bacterial burdens in the lung, substantiating a key role for **CFTR**-mediated bacterial ingestion in lung clearance of P. aeruginosa.

L57 ANSWER 19 OF 25 Elsevier BIOBASE COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2001265513 Elsevier BIOBASE
TITLE: Relationship between I.kappa.B.alpha. deficiency, NF.kappa.B activity and interleukin-8 production in CF human airway epithelial cells
AUTHOR: Tabary O.; Escotte S.; Couetil J.P.; Hubert D.; Dusser D.; Puchelle E.; Jacquot J.
CORPORATE SOURCE: J. Jacquot, INSERM Unite 514, IFR 53, CHU Maison Blanche, 45 rue Cognacq-Jay, 51092 Reims Cedex, France.
E-mail: jacky.jacquot@univ-reims.fr
SOURCE: Pflugers Archiv European Journal of Physiology, (2001), 443/SUPPL. 1 (S40-S44), 16 reference(s)
CODEN: PFLABK ISSN: 0031-6768
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several recent reports have suggested that airway inflammation may precede infection and relate to an endogenous dysregulation of pro-inflammatory cytokines in cystic fibrosis (CF) airways. Evidence suggests that activation of the nuclear factor kappa B (NF.kappa.B), which regulates the inflammatory gene transcription, depends on the degradation of the inhibitory factor I.kappa.B.alpha.. We show that, in in situ human .DELTA.F508 CF bronchial tissues, inhibitor factor I.kappa.B.alpha. is not present in gland cells, although endogenous levels of chemokine IL-8 are high. These data are confirmed by studying cultured CF human bronchial gland cells, in which a lack of cytosolic I.kappa.B.alpha. and high levels of activated NF.kappa.B, concomitant with IL-8 overproduction (a 13-fold increase) are found when compared to non-CF bronchial gland cells. Interestingly, treatment of CF gland cells with the isoflavone genistein, a well known **CFTR** mutant Cl.sup.- channel stimulator, results in a significant decrease ($P<0.001$) in IL-8 production down to levels released by non-CF gland cells. The addition of genistein also reverses the effects of **lipopolysaccharide** (LPS) **Pseudomonas-aeruginosa** -induced nuclear translocation of NF.kappa.B by increasing I.kappa.B.alpha. protein level (65%) in CF gland cells. Our data indicate that the induction of I.kappa.B.alpha. protein in CF airway glandular epithelial cells may be a novel mechanism by which IL-8-mediated lung inflammatory events are markedly reduced in CF patients, at least at the airway glandular level.

L57 ANSWER 20 OF 25 Elsevier BIOBASE COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1996149706 Elsevier BIOBASE
TITLE: How mutant **CFTR** may contribute to **Pseudomonas aeruginosa** infection in cystic fibrosis
AUTHOR: Pier G.B.; Grout M.; Zaidi T.S.; Goldberg J.B.
CORPORATE SOURCE: G.B. Pier, Channing Laboratory, 181 Longwood Ave., Boston, MA 02115-5899, United States.
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996), 154/4 II SUPPL. (S175-S182)
CODEN: AJCMED ISSN: 1073-449X
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Patients with cystic fibrosis (CF) have a pronounced hypersusceptibility

(80 to 90%) to **Pseudomonas aeruginosa** infection. We hypothesized that airway epithelial cell ingestion of bacteria followed by cellular desquamation may protect the lung from infection, and epithelial cells expressing mutant forms of the **cystic fibrosis transmembrane conductance regulator** (**CFTR**) may be defective in this function. We found that transformed human airway epithelial cells homozygous for the .DELTA.F508 allele of **CFTR** were significantly defective in uptake of P. aeruginosa compared with the same cell line complemented with the wild-type allele of **CFTR**. Partial membrane expression of the .DELTA.F508 **CFTR** protein occurs in cells grown at 26.degree. C, and under these conditions uptake of P. aeruginosa occurred at levels comparable to cells with a wild-type allele of **CFTR**. Epithelial cell ingestion assays using isogenic bacterial strains differing in **lipopolysaccharide** (LPS) phenotype, along with inhibition studies, identified the LPS-core oligosaccharide as the bacterial ligand for epithelial cell invasion. Inhibition of epithelial cell ingestion of P. aeruginosa in a neonatal mouse lung infection model led to increased levels of bacteria in the lungs 24 and 48 h after infection. Defective epithelial cell internalization of P. aeruginosa may be a critical factor in hypersusceptibility of CF patients to chronic lung infections.

L57 ANSWER 21 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:996872 SCISEARCH
THE GENUINE ARTICLE: 500GT
TITLE: Relationship between I kappa B alpha deficiency, NF kappa B activity and interleukin-8 production in CF human airway epithelial cells
AUTHOR: Tabary O; Escotte S; Couetil J P; Hubert D; Dusser D; Puchelle E; Jacquot J (Reprint)
CORPORATE SOURCE: CHU Maison Blanche, IFR 53, INSERM Unite 514, 45 Rue Cognacq Jay, F-51092 Reims, France (Reprint); CHU Maison Blanche, IFR 53, INSERM Unite 514, F-51092 Reims, France; Hop Broussais, Dept Chirurg Cardio Vasc, F-75674 Paris, France; Hop Cochin, Serv Pneumol, F-75674 Paris, France
COUNTRY OF AUTHOR: France
SOURCE: PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY, (NOV 2001) Vol. 443, Supp. [1], pp. S40-S44.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.
ISSN: 0031-6768.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 16
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Several recent reports have suggested that airway inflammation may precede infection and relate to an endogenous dysregulation of pro-inflammatory cytokines in cystic fibrosis (CF) airways. Evidence suggests that activation of the nuclear factor kappa B (NF kappaB), which regulates the inflammatory gene transcription, depends on the degradation of the inhibitory factor I kappaB alpha. We show that, in in situ human Delta F508 CF bronchial tissues, inhibitor factor I kappaB alpha is not present in gland cells, although endogenous levels of chemokine IL-8 are high. These data are confirmed by studying cultured CF human bronchial gland cells, in which a lack of cytosolic I kappaB alpha. and high levels of activated NF kappaB, concomitant with IL-8 overproduction (a 13-fold increase) are found when compared to non-CF bronchial gland cells. Interestingly, treatment of CF gland cells with the isoflavone genistein, a well known **CFTR** mutant Cl- channel stimulator, results in a significant decrease (P <0.001) in IL-8 production down to levels released by non-CF gland cells. The addition of genistein also reverses the effects of **lipopolysaccharide** (LPS) **Pseudomonas-**

aeruginosa-induced nuclear translocation of NF kappaB by increasing I kappaB alpha protein level (65%) in CF gland cells. Our data indicate that the induction of I kappaB alpha protein in CF airway glandular epithelial cells may be a novel mechanism by which IL-8-mediated lung inflammatory events are markedly reduced in CF patients, at least at the airway glandular level.

L57 ANSWER 22 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:457047 SCISEARCH
THE GENUINE ARTICLE: 323FT
TITLE: Cytokine dysregulation in activated cystic fibrosis (CF) peripheral lymphocytes
AUTHOR: Moss R B (Reprint); Hsu Y P; Olds L
CORPORATE SOURCE: STANFORD UNIV, MED CTR, DEPT PEDIAT, 701 WELCH RD, NO 3328, PALO ALTO, CA 94304 (Reprint); STANFORD UNIV, SCH MED, DEPT PAEDIAT, PALO ALTO, CA 94304
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (JUN 2000) Vol. 120, No. 3, pp. 518-525.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0009-9104.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recent studies demonstrate in vivo and in vitro cytokine dysregulation in CF epithelial cells. To see if these abnormalities may be generalized to other cells expressing **cystic fibrosis transmembrane conductance regulator** (**CFTR**) but not directly exposed to local inflammation, we studied mRNA transcription, intracellular protein production and extracellular secretion of IL-2, IL-4, IL-5, IL-10 and interferon-gamma (IFN-gamma) from freshly isolated blood mononuclear and CD4(+) T cells from CF patients and controls. Cells were activated by phorbol myristate acetate (PMA) and anti-CD3, PMA-ionomycin, or **lipopolysaccharide** (LPS) and assessed for cytokine mRNA transcription by semiquantitative reverse transcriptase-polymerase chain reaction, intracellular protein production by flow cytometry, and secretion by supernatant ELISA. Cytokine expression was highly stimulus-dependent. CF cells showed higher IL-10 transcription than control cells after maximal activation by LPS (P = 0.01); despite this, cytokine production and secretion were equivalent to controls. CF cells showed lower cellular IL-IO production after PMA-anti-CD3 activation (P = 0.002). CF cells secreted less lFN-gamma than control cells after maximal activation by PMA-anti-CD3 (1836 +/- 273 pg/ml versus 9635 +/- 3437 pg/ml, P = 0.04). IL-2, IL-4 and IL-5 regulation was similar to controls. We conclude that CF mononuclear cells show selective cytokine dysregulation after maximal activation, namely reduced lFN-gamma secretion and increased IL-IO mRNA without increased production or secretion. These findings extend defects described in respiratory epithelial cells to circulating immunoregulatory cells, suggesting a link between CF genotype and cytokine dysregulation.

L57 ANSWER 23 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:486640 SCISEARCH
THE GENUINE ARTICLE: 207VC
TITLE: Early-onset inflammatory responses in vivo to adenoviral vectors in the presence or absence of **lipopolysaccharide**-induced inflammation
AUTHOR: Thorne P S (Reprint); McCray P B; Howe T S; ONeill M A
CORPORATE SOURCE: UNIV IOWA, DEPT PREVENT MED & ENVIRONM HLTH, 100 OAKDALE CAMPUS, 176 IREH, IOWA CITY, IA 52242 (Reprint); UNIV

IOWA, DEPT PEDIAT, IOWA CITY, IA 52242
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY , (JUN 1999) Vol. 20, No. 6, pp. 1155-1164.
Publisher: AMER LUNG ASSOC, 1740 BROADWAY, NEW YORK, NY 10019.
ISSN: 1044-1549.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Adenoviral vectors (Ad) have potential for use in pulmonary gene transfer for treating cystic fibrosis (CF). However, Ad may induce inflammation even in the absence of gene expression. Endotoxin from gramnegative bacteria in the airways of CF patients may also induce inflammation, and may further inhibit vector: delivery and gene transfer. We used a mouse model to study the time course of Ad-induced lung inflammation and to assess additivity with **lipopolysaccharide** (LPS)-induced inflammatory responses. C3H/HeJ endotoxin-resistant (RES) mice hyporesponsive to inflammatory stimuli and normoresponsive C3HeB/FeJ endotoxin-sensitive (SEN) mice were studied to characterize inflammatory responses that follow intratracheal instillation of inactivated Ad, with or without simultaneous inhalation exposure to LPS, Instillation of 10(10) Ad particles dramatically increased bronchoalveolar lavage fluid (BALF) concentrations of tumor necrosis factor (TNF)-alpha and interleukin (TL)-6 at 3 to 6 h and induced profound neutrophilia, maximal at 12 to 24 h, SEN mice had tenfold greater responses than did RES mice at 6, 12, and 24 h. Mice exposed to Ad alone, LPS alone, or Ad + LPS had significant inflammation at the 3-h time point as demonstrated by BALE neutrophils, TNF-alpha, and IL-6, With all three treatments, SEN mice had a five- to 300-fold greater response than did RES mice, Importantly, Ad + LPS yielded no greater inflammatory response than LPS without Ad. These data demonstrate that replication-deficient Ad induce early inflammation and LPS-induced inflammation is not augmented by concurrent treatment with Ad.

L57 ANSWER 24 OF 25 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 97:901990 SCISEARCH
THE GENUINE ARTICLE: YJ227
TITLE: Altered cytokine production by cystic fibrosis tracheal gland serous cells
AUTHOR: Kammouni W; Figarella C; Marchand S; Merten M (Reprint)
CORPORATE SOURCE: FAC MED MARSEILLE, GRP RECH GLANDES EXOCRINES, 27 BLVD JEAN MOULIN, F-13385 MARSEILLE 05, FRANCE (Reprint); FAC MED MARSEILLE, GRP RECH GLANDES EXOCRINES, F-13385 MARSEILLE 05, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: INFECTION AND IMMUNITY, (DEC 1997) Vol. 65, No. 12, pp. 5176-5183.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Human submucosal tracheal glands are now believed to play a major role in the physiopathology of cystic fibrosis (CF). We successfully developed techniques for culturing human tracheal gland serous cells from normal individuals (HTGS cells) and from CF patients (CF-HTGS cells) and have shown that the cultured cells have retained most of their in vivo epithelial and secretory characteristics. In order to determine to what

extent the serous cells may participate in the lung defense against infection, we examined the effects of the **lipopolysaccharide** (LPS) of **Pseudomonas aeruginosa** on HTGS and CF-HTGS cells, with special reference to tumor necrosis factor alpha (TNF-alpha), interleukin-6 (IL-6), and IL-8 secretion. HTGS cells showed a daily basal secretion of IL-6 (1.68 +/- 0.14 ng/10(6) cells) and IL-8 (9.6 +/- 1.3 ng/10(6) cells) and no constitutive secretion of TNF-alpha. Treatment with P. aeruginosa LPS resulted in a significant increase in the basal production of IL-6 (increase of 200% +/- 12%) and IL-8 (525% +/- 40%) as well as a rapid production of TNF-alpha (250 +/- 38 pg/10(6) cells). The LPS-induced secretion of IL-6 and IL-8, but not that of TNF-alpha, was inhibited by glucocorticoids, CF-HTGS cells showed a much higher basal secretion of IL-6 (13.2 +/- 0.5 ng/10(6) cells) and IL-8 (45.6 +/- 7.2 ng/10(6) cells) than normal cells. Treatment with the LPS of P. aeruginosa induced increased production of IL-6 (increase of 100% +/- 8%) and IL-8 (55% +/- 18%) but did not induce the secretion of TNF-alpha. Neither intracellular TNF-alpha nor TNF-alpha transcripts were found in CF-HTGS cells, whereas they were found in normal HTGS cells. In addition, dexamethasone was found to stimulate IL-6 and IL-8 secretion (in the presence or absence of LPS) but did not induce any secretion of TNF-alpha. All these data indicate that HTGS cells are responsive to P. aeruginosa LPS, which results in an increased secretion of IL-6, IL-8, and TNF-alpha, the secretion of which appeared to he impaired in CF-HTGS cells.

L57 ANSWER 25 OF 25 USPATFULL

ACCESSION NUMBER:	2002:48024 USPATFULL
TITLE:	NOVEL VACCINES AND PHARMACEUTICAL COMPOSITIONS USING MEMBRANE VESICLES OF MICROORGANISMS, AND METHODS FOR PREPARING SAME
INVENTOR(S):	KADURUGAMUWA, JAGATH L., GUELPH, CANADA BEVERIDGE, TERRY J., ELORA, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002028215	A1	20020307	
APPLICATION INFO.:	US 1999-370860	A1	19990809	(9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	DOUGLAS P MUELLER, MERCHANT & GOULD PC, 3100 NORWEST CENTER, 90 SOUTH SEVENTH STREET, MINNEAPOLIS, MN, 55402
NUMBER OF CLAIMS:	17
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	35 Drawing Page(s)
LINE COUNT:	2647

AB The invention relates to novel vaccines and pharmaceutical compositions using membrane vesicles of microorganisms, methods for preparing same, and their use in the prevention and treatment of infectious diseases.

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